

PATENT COOPERATION TREATY

PCT

REC'D 26 APR 2001

VIDEO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference PF-0585 PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/20239	International filing date (day/month/year) 01 SEPTEMBER 1999	Priority date (day/month/year) 03 SEPTEMBER 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant INCYTE PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 29 MARCH 2000	Date of completion of this report 06 MARCH 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>PREMA MERTZ</i> PREMA MERTZ
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/20239

**I. Basis of the report**1. With regard to the **elements** of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-47, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

- ☒ the claims:  
pages 48-49, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

- ☒ the drawings:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

- ☒ the sequence listing part of the description:  
pages 1-3, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/20239

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims	<u>15, 17-20</u>	YES
	Claims	<u>1-14, 16</u>	NO
Inventive Step (IS)	Claims	<u>17-20</u>	YES
	Claims	<u>1-16</u>	NO
Industrial Applicability (IA)	Claims	<u>1-20</u>	YES
	Claims	<u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

Claims 1-14, 16 lack novelty under PCT Article 33(2) as being anticipated by Morgan et al. (1996).

Morgan et al. disclose a DNA encoding a Slim protein which is a novel family of LIM-proteins expressed in skeletal muscle (pages 632-638). Therefore, the DNA encoding a fragment of the polypeptide of the reference, would potentially be a single amino acid. The reference also discloses that the DNA encoding the enzyme was cloned into an expression vector, host cells were transformed with the DNA in the vector. A fragment of the DNA of the reference would potentially be any nucleotide capable of selectively hybridizing to the polynucleotide of SEQ ID NO:2 described in the instant application. Therefore, the DNA sequence disclosed in the reference meets the limitations of a DNA molecule encoding a fragment of SEQ ID NO:1.

Claim 15 lacks an inventive step under PCT Article 33(3) as being obvious over Morgan et al. (1996).

The disclosure of Morgan et al has been set forth above. However, Morgan fails to teach a pharmaceutical composition comprising the slim protein and a method of treatment with the protein.

It would have been prima facie obvious to one of ordinary skill in the art, at the time of the instant invention to obtain the protein in a physiological carrier such as phosphate-buffered saline for administering therapeutically for its intended use.

Claims 17-20 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest an agonist, an antagonist and a method of treatment of a disorder by administering LIM domain protein homologs (LDPH) or antagonists of LDPH.

In the communication filed in Paper No. 15 (14/2/01) in response to the Written Opinion, Applicants have traversed the objections by the Examiner but have failed to provide any arguments or demonstrate the error in the objections by the Examiner and therefore the objections are maintained.  
(Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/20239

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): A61K 38/17, 38/18; C07K 14/435, 14/47, 14.475, 16/18; C12Q 1/68; C12N 5/10, 15/12, 15/16, 15/63, 15/64  
and US Cl.: 536/23.1, 23.5, 24.3, 24.31; 530/350, 387.1, 387.9; 435/ 6, 69.1, 71.1, 71.2, 471, 325, 252.3, 254.11,  
320.1; 514/2, 8/12

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

----- NEW CITATIONS -----

NONE

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 02 August 2000 (02.08.00)	
<b>International application No.</b> PCT/US99/20239	<b>Applicant's or agent's file reference</b> PF-0585 PCT
<b>International filing date (day/month/year)</b> 01 September 1999 (01.09.99)	<b>Priority date (day/month/year)</b> 03 September 1998 (03.09.98)
<b>Applicant</b> TANG, Y., Tang et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
29 March 2000 (29.03.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer Pascal Piriou</p> <p>Telephone No.: (41-22) 338.83.38</p>
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# INTERNATIONAL SEARCH REPORT

onal Application No

PCT/US 99/20239

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 A61K38/17 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MORGAN M J ET AL.: "Slim defines a novel family of LIM-proteins expressed in skeletal muscle" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 225, no. 2, 14 August 1996 (1996-08-14), pages 632-638, XP002126624	1-14, 16
Y	Note: 95.7% aa sequence identity of SLIM2 with SEQ ID NO:1 in 280 aa overlap, 98.3% nt sequence identity with SEQ ID NO:2 in 1510 bp overlap. abstract page 632, paragraph 3 page 633, paragraph 3 figures 3,4 --- -/--	15, 19



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

23 December 1999

Date of mailing of the international search report

24/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040. Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

van de Kamp, M

## INTERNATIONAL SEARCH REPORT

Original Application No.

PCT/US 99/20239

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL EMBL ID HSB02C091, AC Z19178, 1 January 1993 (1993-01-01) GENEXPRESS: "H. sapiens partial cDNA sequence; clone 02C09; strand (-), single read" XP002126614	1-14, 16
Y	Note: 100.0% aa sequence identity of Z19178 with SEQ ID NO:1 in 99 aa overlap, 99.0% nt sequence identity with SEQ ID NO:2 in 315 bp overlap. the whole document	15, 19
A	-& AUFRAY C ET AL.: "IMAGE: intégration au niveau moléculaire de l'analyse du génom humain et de son expression / IMAGE: integrated molecular analysis of the human genome and its expression" C.R. ACAD. SCI. PARIS, SCIENCES DE LA VIE/LIFE SCIENCES, GÉNÉTIQUE/GENETICS, vol. 318, 1995, pages 263-272, XP000579830 abstract page 265, left-hand column, line 43-45 ----	1-14
Y	WO 98 18822 A (INCYTE PHARMA INC ;BANDMAN OLGA (US); GOLI SURYA K (US); HILLMAN J) 7 May 1998 (1998-05-07) page 3, line 8-13 page 31, line 30 -page 35, line 15 claims 45,49 ----	15, 19
A	DAWID I B ET AL: "LIM domains: multiple roles as adapters and functional modifiers in protein interactions" TRENDS IN GENETICS,NL,ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, vol. 14, no. 4, April 1998 (1998-04), page 156-162 XP004112319 ISSN: 0168-9525 the whole document -----	1-14

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 20239

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark (1): Although claim 19  
is directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☒ Claims Nos.: 17, 18, 20  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:  
See FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims: it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



## INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 99 /20239

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 17, 18, 20

Remark (2): Claims 17, 18 and 20 refer to agonists and antagonists of the polypeptide without giving a true technical characterisation. Moreover, no specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/20239

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9818822 A	07-05-1998	US 5863898 A	26-01-1999
		AU 4824197 A	22-05-1998
		EP 0931095 A	28-07-1999
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PF-0585 PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 20239</b>	International filing date (day/month/year) <b>01/09/1999</b>	(Earliest) Priority Date (day/month/year) <b>03/09/1998</b>
Applicant  <b>INCYTE PHARMACEUTICALS, INC. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the language, the International search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.

☐ the International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, the International search was carried out on the basis of the sequence listing:

☒ contained in the International application in written form.

☐ filed together with the International application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 20239

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark (1): Although claim 19  
is directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☒ Claims Nos.: 17, 18, 20  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:  
See FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 17, 18, 20

Remark (2): Claims 17, 18 and 20 refer to agonists and antagonists of the polypeptide without giving a true technical characterisation. Moreover, no specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.